ARGUMENTS/REMARKS

Claim 1-47 and 51-66 are currently pending in this application. Claims 3, 21-47, 51-57 and 60-64 have been canceled as directed to non-elected subject matter, without admission and without prejudice to Applicants' right to pursue the subject matter of those canceled claims in either this or other (*e.g.*, related continuing or divisional) patent applications. Claim 1 has also been canceled without prejudice or admission. Claims 2, 4-9, 11-19, 58-59 and 65 have been amended so that they now depend from independent claim 66 rather than from canceled claim 1. Hence, no new matter has been introduced in these amendments.

Upon entry of these amendments. Claims 2-20, 56-59 and 65-66 will be pending. Entry and consideration of these amendments is respectfully requested.

Election/Restriction

Claims 3, 21-47, 51-57 and 60-64 are directed to subject matter that was not elected in Applicants' response to the Restriction Requirement for this application. The Office Action indicates that a complete response to the Office Action "must include a cancellation of non-elected claims or other appropriate action." See, in the Office Action, at page 2, lines 9-10. Accordingly, claims 3, 21-47, 51-57 and 60-64 have been canceled in this amendment. However, the cancellation of these claims is made without admission and without prejudice to Applicants' rights to traverse the Requirement for Restriction and/or pursue the subject matter of the non-elected claims in either this or other (*e.g.*, related continuation or divisional) patent applications.

The Rejections Under the First Paragraph of 35 U.S.C. § 112 Should Be Withdrawn

Claim 1-2, 4-20, 58-59 and 65 have been newly rejected as failing to comply with the Written Description Requirement set forth in 35 U.S.C. § 112, first paragraph. In particular, the Examiner argues that "there is no support [in the specification] for the newly added negative proviso" introduced by Applicants' previous amendment to claim 1. In response, Applicants

respectfully point out that claim 1 has been canceled, without prejudice or admission. The other claims rejected under the first paragraph of 35 U.S.C. 112 (*i.e.*, claims 2, 4-20, 58-59 and 65) have been amended so that they now depend from claim 66. Applicants therefore respectfully submit that the rejections under the first paragraph of 35 U.S.C. § 112 have been obviated, and should be withdrawn.

The Claim Rejection Under 35 U.S.C. § 102
Should Be Withdrawn

The Examiner has maintained her rejection of claim 1-2, 4-8, 11-13, 16, and 58-59 under 35 U.S.C. 102(e), as being anticipated by U.S. Patent No. 6,448,389 to *Gonczol et al.* ("*Gonczol*"). Claim 66, which was added in Applicant's previous amendment, also stands rejected as anticipated by *Gonczol*. In particular, the Examiner argues that *Gonczol* anticipates these claims because, according to the Examiner, "*Gonczol et al.* teach a vaccine formulation comprising DNA molecules expressing gB (an antigen) to induce immune response to HCMV...[and] also teach[es] suspending the DNA formulations in pharmaceutically acceptable carriers and incorporating a magnesium hydroxide adjuvant." See, in the Office Action, at page 4, lines 10-14.

At the outset, Applicants wish to respectfully point out that claim 1 has been canceled in this amendment, without prejudice or admission, and in favor of independent claim 66. The rejected dependent claims (*i.e.*, claims 2, 4-8, 11-13, 16, and 58-59) have been amended so that they now depend, either directly or indirectly, from claim 66. Hence, of the claims which will be pending upon entry of this amendment, only claims 2, 4-8, 11-13, 16, 58-59 and 66 stand rejected as anticipated by *Gonczol*.

The Examiner argues that *Gonczol* anticipates these claims, because it describes a vaccine formulation comprising DNA molecules expressing a particular antigen (gB protein). Hence, the vaccine formulations described by *Gonczol* do not, themselves, contain an antigen. Rather, they contain DNA coding for a particular antigen, gB protein. Claim 66, however, specifically recites a parenteral vaccine formulation that comprises "at least one immunogenic

substance selected from the group consisting of antigens, allergens, allergoids, peptides, proteins, haptens, carbohydrate, PNA and RNA." The claim does not recite vaccine formulations containing ***any*** DNA molecule - either as an antigen itself, or encoding a particular antigen (as described by *Gonczol*).

For the foregoing reason, Applicants submit that the Examiner's rejection of claims 1,2, 4-8, 11-13, 16, 58-59 and 66 under 35 U.S.C. 102 has been obviated, and respectfully request that the rejection be withdrawn.

The Rejections For Obviousness

Should Be (Withdrawn)

The Examiner has also rejected the pending claims under 35 U.S.C. 103(a), as being obvious over various combinations of cited references. Each of these rejections is discussed, in turn, below.

(i) Claims 9, 10, and 20

The Examiner has sustained the rejection of these claims as unpatentable over *Gonczol* in view of *Vogel et al.* ("A Compendium of Vaccine Adjuvants and Excipients" in Vaccine Design: The Subunit and Adjuvant Approcah (Chapter 7), M.F. Powell & M.J. Newmann, Eds. (Plenum Press, New York) 1995, pages 141-228). As explained above, however, *Gonczol* merely teaches vaccines containing a DNA that encodes a particular antigen. Neither *Gonczol* nor *Vogel* teaches or suggests vaccines containing any of the antigens recited in pending claim 66 of this application. Applicants therefore respectfully submit that this rejection should be withdrawn.

(ii) Claims 1-2, 4-8, 11-13, 58-59, and 66

The Examiner has maintained the rejection of claims 1, 2, 4-8, 11-13, and 58-59 and rejected newly presented claim 66 as being unpatentable over *Aviram et al.* (U.S. 6,362,236) and *Conte et al.* (U.S. 5,464,633). According to the Examiner, *Conte* specifically provides the teaching that titanium

dioxide is an adjuvant. In contrast, the Applicants have asserted that *Conte* teaches that titanium dioxide is an opacity agent, a contention that the Examiner has rejected.

The Applicants respectfully traverse this rejection and request reconsideration. Based on a reexamination of the *Conte* patent, the Applicants suggest that the critical issue, which has been overlooked, is the meaning of the word "adjuvant" *as it is used in Conte.* As the analysis below will show, the term has a very general meaning in *Conte,* akin to "additive" or "ingredient" – that is in marked contrast to the specialized immunological definition of "adjuvant" in the instant application.

The instant application provides a basic definition of adjuvant that is well recognized by one skilled in the art of immunology and vaccination: "substances that, when administered together with an antigen, have the capacity to augment the immune response to the antigen." p. 1, ll. 16-18.

Conte does not provide a formal definition of "adjuvant," requiring extraction of the meaning from its use in the patent. As a guiding principle, §2141.02 of the MPEP states that a prior art reference must be considered in its entirety, including portions that would lead away from the claimed invention (citing W.L. Gore & Associates, Inc. v. Garlock, Inc.., 721 F.2d 1540 (Fed Cir. 1983)).[1] Reflecting this broad consideration are the following exemplary passages, including that cited by the Examiner:

> (1) Col. 4, ll. 41-45 (emphasis added):
> In addition *adjuvant* substances ***as*** natural and/or synthetic polymeric materials belonging to the class of so called *gellable polymers, able to slow the release* of the active substance from the core, may be used.
>
> (2) Col. 5, ll. 58-67 (emphasis added):
> In the case said external layer is applied by compression diluents ***as*** those traditionally used in the solid forms preparation or fatty, waxy, natural and synthetic or semisynthetic substances ***as*** glyceryl monostearate and semisynthetic triglyceride derivatives, semisynthetic glycerides, hydrogenated castor oil, glycerylpalmitostearate, glyceryl behenate *and other adjuvants* such as *binders* ***as*** polyvinylpyrrolidone, gelatin, ethylcellulose, methylcellulose, sodium carboxymethylcellulose and other natural or synthetic substances well known to the skilled in the field, may be used

[1] Applicants respectfully submit that this need is especially critical in the analysis of *Conte*, given that English is clearly not the first language of the drafters.

(3) Claim 9:
Tablet as claimed in claim 1, characterized in that said *adjuvant* substances of the core are *hydrophobic diluents* selected from the group consisting of glyceryl monostearate, hyrdogenated castor oil, waxes, and glycerides.

(4) Col. 6, ll. 12-17 (the subsection cited by Examiner is underlined):
In such case besides the basic polymeric material as before described *plasticizing substances* ***as*** butylphthalate, propylphthalate, dietylphthalate, zein, polyoxyethylenglycols with different molecular weight and opacity agents ***as*** titanium dioxide and other adjuvants well known to the skilled in the field, may be used.

These passages, which are consistent with the remainder of the reference, leave no question that "adjuvant" is used in a different way by *Conte* than by the Applicants and others of ordinary skill in the immunological arts. First, passages 1-3 reveal that the meaning of adjuvant in *Conte* specifically includes a number of pharmaceutical additives, including slow release compounds, binders, and hydrophobic diluents. Second, the language of these passages is only consistent by substituting "such as" for "as". Third, this heightened perspective permits ready reconciliation of disputed passage 4, by revealing that "adjuvant" refers to many different additives and ingredients, including opacity agents.

A broad examination of *Conte* therefore reveals that the term "adjuvant" does not have the same meaning as is has in the instant application. Rather, it has a broad meaning most akin to a "general pharmaceutical additive." Moreover, this definition is also consistent with the general teaching of *Aviram et al.* that titanium dioxide is a common excipient or carrier. In this sense, then, both the Examiner and Applicants are correct. Titanium dioxide is an opacity agent specifically, but when in the special pharmaceutical context of *Conte*, is also an example of an "adjuvant" or pharmaceutical additive.

For these reasons, Applicant assert that *Conte* does not teach that titanium dioxide is an "adjuvant" as that term by the Applicants and others skilled in the art of immunology: it is not an immunological compound capable of specifically augmenting an immune reponse. Consequently, the combination of asserted references does not teach all elements of the claimed inventions. Accordingly, Applicants respectfully request that the obviousness rejections be withdrawn.

(ii) Claims 14, 15, 19, and 65

The Examiner has rejected these claims as being unpatentable over the combination of (1) *Gonczol* or *Aviram*; and (2) *Conte et al.* The Applicants traverse these rejection on the basis of the claim amendments and arguments just presented. *Gonczol* and *Conte* do not teach the elements of the claimed formulations. Accordingly, the Applicants respectfully request withdrawal of this rejection.

Miscellaneous Claim Objections

Applicants note, with appreciation, that the Examiner has found the subject matter of claim 17 to be allowable. However, the Examiner has objected to this allowable claim as being dependent upon a rejected base claim – *i.e.*, claim 1. The Office Action indicates, however, that claim 17 "would be allowable if rewritten in independent form, including all of the limitations of the base claim and any intervening claims. See, in the Office Action, at page 9, lines 15-17.

In response, Applicants note that claim 1 has been canceled without prejudice or admission in this amendment. Claim 17 has been amended so that it now depends from claim 66. As explained in detail above, Applicants maintain that the subject matter of claim 66 is fully allowable and that the Examiner's objections to that claim have been overcome. Hence, claim 17, as amended, is also allowable. For this reason, Applicants respectfully decline to amend claim 17 as suggested in the Office Action, and respectfully submit that the Examiner's objections to that claim should be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

Respectfully submitted,

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By Samuel S. Woodley

Samuel S. Woodley, Ph.D.
Registration No.: 43,287
DARBY & DARBY P.C.
P.O. Box 5257
New York, New York 10150-5257
(212) 527-7700
(212) 753-6237 (Fax)
Attorneys/Agents For Applicant